

### REMARKS

Claims 38, 40, 41, 43, 45, 46, 49, and 65-68 are pending and stand rejected under 35 U.S.C. 112, first paragraph (written description and enablement).

Claims 38, 40 and 65 have been amended as shown above to explicitly specify the control elements of the expression cassettes. Thus, the amendments make explicit what was previously implicit. (*See, e.g.*, pages 35-41 (Section 3.1.1)). Reconsideration of the application in view of the foregoing amendments and following remarks is respectfully requested.

#### 35 U.S.C. §112, First Paragraph, Written Description

Claims 38 and 65-68 remain rejected on the grounds that Applicants' specification fails to sufficiently describe the claimed transgenic mice. (Final Office Action, pages 2-3).

In order to satisfy the written description requirement of 35 U.S.C. § 112, first paragraph, it is sufficient that the specification reasonably convey to a skilled artisan that Applicants' were in possession of the claimed invention at the time of filing. *See, e.g., In re Wertheim*, 191 USPQ 90 (CCPA 1976).

The pending claims are directed to transgenic mice containing the specified expression cassettes. In particular, the pending claims set forth particular control elements derived from particular genes and sequences. For the reasons of record and those presented herein, the specification as filed more than adequately describes and details relevant identifying characteristics of the animals of pending claims 38 and 65-68. Indeed, the specification sets forth particular control elements derived from stress-inducible genes or containing the specified control response element. (*See, e.g.*, Section 3.1.1. *et seq.* starting on page 35). Furthermore, production of expression cassettes and transgenic mice containing these expression cassettes is also described in detail. (*e.g.*, Section 4.0). Ample structure and identifying characteristics of the mice are provided so that a skilled artisan would recognize that Applicants were in possession of the claimed invention. The claims are not directed to a huge genus, but, rather, to rodents precisely defined by both their structure and their phenotype.

Thus, the specification as filed more than adequately describes the claimed mice by the claimed structural, functional and physical characteristics. Accordingly, withdrawal of this rejection is respectfully requested.

#### 35 U.S.C. §112, First Paragraph, Enablement

The Examiner maintains that undue experimentation would be required in order to practice the invention of claims 38, 40, 41, 43, 45, 46, 49 and 65-68. (Final Office Action, pages 3-4). As with written description, the Examiner asserts that both the transgenic mice comprising

a panel of expression cassettes themselves and methods of determining the effect of an analyte using these mice would have required undue experimentation and was unpredictable.

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). Accordingly, in the pending case, Applicants are in no way required to predict the phenotype of each and every transgenic mouse containing the claimed panels of expression cassettes. All that is required is that the specification teaches a skilled practitioner how to select a control element from the genes and response elements set forth in the claims; operably link the sequence to a sequence encoding a light-generating protein; and use the control element-coding sequence construct to create a transgenic animal. The specification provides more than adequate guidance in all these regards.

As noted above, the specification teaches structure and characteristics of all the recited control elements. (See, e.g., Section 3.1.1 of the specification). These control elements (or genes from which they are derived) were well known at the time of filing. Cloning of any of the recited control sequences to a light-generating encoding sequence would also be absolutely straightforward and, indeed, working examples are provided in the specification. Finally, making transgenic animals was also straightforward at the time the specification was filed and the specification provides further guidance in this regard.

The test of enablement is not what is predictable, but what the specification teaches the skilled practitioner in regard to the claimed subject matter. Not every species encompassed by the claims, even in an unpredictable area like the chemical sciences, needs to be disclosed. (*In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219, CCPA 1976.) The notion that one of ordinary skill in the art must have reasonable assurance of obtaining an active claimed product has been emphatically rejected (*Angstadt* at 219). So long as it is clear that some species render a composition operative, the inclusion of some possible inoperative species does not invalidate the claim under paragraph 1, of 35 U.S.C. §112. (*In re Cook*, 439 F.2d 730, 735, 169 USPQ 298, CCPA 1971; *Horton v. Stevens*, 7 USPQ2d 1245, 1247, Fed. Cir. 1988.) Further, even evidence of the need for some experimentation does not invalidate a claim on ground of undue experimentation, nor does it fulfill the PTO's burden of proof. (*In re Angstadt* at 504; *In re Morehouse*, 545 F.2d 162, 165, 192 USPQ 29,32, CCPA 1976.)

The Examiner's contention that the specification does not provide adequate guidance in regards to the pending claims is also legally untenable. A low success rate of integration and function does not mean that the specification is non-enabling, as illustrated in a recent, unpublished opinion, the Board of Patent Appeals and Interferences, *Ex parte Chen* 61 USPQ2d 1026 (BPAI 2001, unpublished). With regard to enablement, the Board rejected the Examiner's

conclusion that a 1% success rate in producing the claimed transgenic carp indicated that the experimentation need to produce the transgenic fish was undue:

The examiner's concerns relating to reproducibility of the exact carp, phenotype characteristics, levels of expression and reproducibility of identical fish are misplaced, because the claims do not include or require these limitations. The appellants need only provide an enabling disclosure for the claimed invention. [citing *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991) and *In re Fisher*, 166 USPQ 18 (CCPA 1970)]. Thus, there is no requirement for a disclosure of what the examiner perceives as possible characteristics of such a product. *Ex parte Chen*, 61 USPQ2d at 1028 (BPAI 2002, unpublished).

The Board also found that Chen's disclosure was sufficient:

We remind the examiner that some experimentation may be required as long as it is not undue. [citation to *Vaeck* omitted]. Appellants' disclosure explicitly describes the methodology used to arrive at the claimed transgenic carp. As the record now stands, the numbers emphasized by the examiner would reasonably appear to reflect the need for a repetitive procedure, rather than undue experimentation by those wishing to practice the invention. *Id.*

As in *Chen*, one of the skill in the art could readily follow Applicants' explicit disclosure regarding how to make the claimed transgenic rodents and determine whether the rodents exhibited the required phenotype. As the Board has made plain, repetitious experimentation is not necessarily undue experimentation.

By requiring prediction of the phenotype of the claimed rodents, the Office has not applied the proper enablement standard. It is axiomatic that working examples are **never** required in order to show enablement. See, MPEP 2164.02. Under the proper enablement standard, it is plain that the specification as filed makes it routine for the skilled worker to make and use the claimed mice.

Even Patent Office Training materials recognize that claims to transgenic animals are fully enabled where "an enabled use for the claimed transgenic mouse is well established." (See, Training Materials for Examining Patent Applications with Respect to 35 U.S.C. 112, first paragraph -- Enablement, Example I, page I-6, *circa* 1997). In the case at hand, an enabled use for transgenic animals comprising expression cassettes encoding a light-generating protein is well established, as evidenced for example by U.S. Patent No. 6,217,847 which shows the generation of a transgenic animal comprising an expression cassette encoding luciferase and use of these animals for the temporal and spatial analysis of transcriptional control.

When the enablement requirement is determined relative to the pending claims, it is clear that the specification enables the skilled artisan to make and use the claimed rodents.


### CONCLUSION

Applicant respectfully submits that the claims comply with the requirements of 35 U.S.C. §112 and define an invention that is patentable over the art. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

If the Examiner notes any further matters that the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned at (650) 843-5608.

Respectfully submitted,

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